4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2012-P-1034]

Determination That SUBOXONE (Buprenorphine Hydrochloride and Naloxone Hydrochloride) Sublingual Tablets, 2 Milligrams/0.5 Milligrams and 8 Milligrams/2 Milligrams, Were Not Withdrawn From Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) has determined that SUBOXONE (buprenorphine hydrochloride (HCl) and naloxone HCl) sublingual tablets, 2 milligrams (mg)/0.5 mg and 8 mg/2 mg, were not withdrawn from sale for reasons of safety or effectiveness. This determination will allow FDA to approve abbreviated new drug applications (ANDAs) for buprenorphine HCl and naloxone HCl sublingual tablets, 2 mg/0.5 mg and 8 mg/2 mg, if all other legal and regulatory requirements are met.

FOR FURTHER INFORMATION CONTACT: David E. Markert, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 6248, Silver Spring, MD 20993-0002, 301-796-3602.

SUPPLEMENTARY INFORMATION:

I. Background

In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 98-417) (the 1984 amendments), which authorized the approval of duplicate versions of drug products under an ANDA procedure. ANDA applicants must, with

certain exceptions, show that the drug for which they are seeking approval contains the same active ingredient in the same strength and dosage form as the "listed drug," which is a version of the drug that was previously approved. ANDA applicants do not have to repeat the extensive clinical testing otherwise necessary to gain approval of a new drug application (NDA).

The 1984 amendments include what is now section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)), which requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the "Approved Drug Products With Therapeutic Equivalence Evaluations," which is known generally as the "Orange Book." Under FDA regulations, drugs are removed from the list if the Agency withdraws or suspends approval of the drug's NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).

A person may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale, but must be made prior to approving an ANDA that refers to the listed drug (§ 314.161 (21 CFR 314.161). FDA may not approve an ANDA that does not refer to a listed drug.

SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual tablets, 2 mg/0.5 mg and 8 mg/2 mg, are the subject of NDA 20-733, held by Reckitt Benckiser Pharmaceuticals, Inc. (Reckitt), and initially approved on October 8, 2002. SUBOXONE is indicated for maintenance treatment of opioid dependence.

In a letter dated September 18, 2012, Reckitt notified FDA that SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual tablets, 2 mg/0.5 mg and 8 mg/2 mg, were being discontinued. Shortly thereafter, Reckitt publicly announced that it was discontinuing this

product for safety reasons and that it had submitted a citizen petition requesting that FDA require all manufacturers of buprenorphine-containing products for the treatment of opioid dependence to implement certain public health safeguards (Ref. 1).[1] Reckitt later informed the Agency that it ceased distributing SUBOXONE sublingual tablets in March 2013, at which time FDA moved the product to the "Discontinued Drug Product List" section of the Orange Book.

Lachman Consultant Services, Inc. (Lachman), submitted a citizen petition dated September 27, 2012 (Docket No. FDA-2012-P-1034), under 21 CFR 10.30, requesting that the Agency determine whether SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual tablets, 2 mg/0.5 mg and 8 mg/2 mg, were withdrawn from sale for reasons of safety or effectiveness. The petitioner noted that Reckitt had publicly announced that it was discontinuing this product.

After considering Lachman's citizen petition and reviewing our records, including the safety analysis that the Agency prepared in connection with Reckitt's citizen petition, FDA has determined under § 314.161 that SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual tablets, 2 mg/0.5 mg and 8 mg/2 mg, were not withdrawn for reasons of safety. We described the basis for this determination in our letter response to Reckitt's citizen petition (available at http://www.regulations.gov under Docket No. FDA-2012-P-1028). Since the issuance of that response, we have updated our reviews of relevant literature and data on this product. We found no additional information during this process that would indicate that

[1] The citizen petition (Docket No. FDA-2012-P-1028), which was submitted on September 25, 2012, also requested that FDA refuse to approve any ANDAs for buprenorphine HCl and naloxone HCl products for opioid dependence until the Agency determined whether SUBOXONE sublingual tablets were discontinued for safety reasons. In its February 22, 2013, response to the citizen petition, FDA concluded that this request was premature because Reckitt had not yet withdrawn SUBOXONE sublingual tablets from sale. Nonetheless, the Agency conducted a full review and analysis of the safety issues raised in Reckitt's citizen petition and determined, on the basis of the data available at that time, that withdrawal of SUBOXONE sublingual tablets from sale was not necessary for reasons of safety.

SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual tablets, 2 mg/0.5 mg and 8 mg/2 mg, were, or should have been, withdrawn from sale for reasons of safety.

FDA has also determined under § 314.161 that SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual tablets, 2 mg/0.5 mg and 8 mg/2 mg, were not withdrawn for reasons of effectiveness. We have reviewed our records and other relevant data sources, and have found no information that would indicate that this product was ineffective as a maintenance treatment of opioid dependence.

Accordingly, the Agency will continue to list SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual tablets, 2 mg/0.5 mg and 8 mg/2 mg, in the "Discontinued Drug Product List" section of the Orange Book. The "Discontinued Drug Product List" delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness. ANDAs that refer to SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual tablets, 2 mg/0.5 mg and 8 mg/2 mg, may be approved by the Agency as long as they meet all other legal and regulatory requirements for the approval of ANDAs. If FDA determines that labeling for this drug product should be revised to meet current standards, the Agency will advise ANDA applicants to submit such labeling.

II. References

The following reference has been placed on display in the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday, and is available electronically at http://www.regulations.gov. (FDA has verified the Web site address in this reference section, but FDA is not responsible for any subsequent changes to the Web site after this document publishes in the Federal Register.)

1. “Further US RB Pharmaceuticals Announcement,”

http://www.rb.com/site/rkbr/templates/mediainvestorsgeneral2.aspx?pageid=1332&cc=GB,

Reckitt Benckiser Group plc, September 25, 2012. Web. May 17, 2013.

Dated: May 31, 2013.

Janet Woodcock,

Director,

Center for Drug Evaluation and Research.

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